

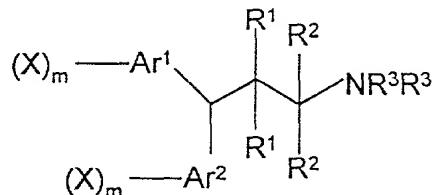
Claims

1. A method of treating a patient for depression comprising the step of administering to said patient an effective amount of a compound having a NMDA IC_{50} of about 50 nM to about 1 μ M as measured in the NMDA assay and a serotonin reuptake IC_{50} of less than or equal to about 100 nm as measured in the serotonin reuptake inhibition assay.

2. The method of claim 1, wherein said compound has an NMDA receptor IC_{50} of 50 nM to 1 μ M and a SSRI IC_{50} less than 100 nM.

3. A method of treating a patient for depression comprising the step of administering to said patient an effective amount of a compound having the chemical structure:

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wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, and -O-acyl;

Ar¹ and Ar² are each independently selected from the group consisting of phenyl, naphthyl, thiofuranyl, tetrahydronaphthyl, furanyl, tetrahydrofuranyl, pyridyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, cyclohexyl, cycloheptyl, and cyclopentyl;

each R¹ is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R² is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R²'s together are imino;

each R^3 is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl; and each m is independently an integer from 0 to 5; provided that if both R_3 's are -CH₃, then both X_m 's are not 5 3-F, 4-F, 3-CF₃, 4-Cl, and if both R_3 's are -CH₃, and one X_m is 4-F then the other X_m is not 4-Cl; further provided that if one R_3 is -H and the other R_3 is -CH₃ then both X_m 's are not 4-Cl, and if one R_3 is -H and the other R_3 is -CH₃ then at least one m is 1; or a pharmaceutically acceptable salt thereof.

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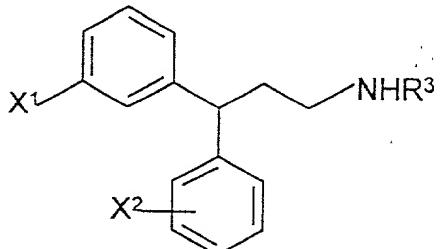
4. The method of claim 3 wherein for said compound each X is independently either -F, -Cl, -OCF₃ or -CF₃;

each R^1 is -H;

each R^2 is -H;

15 one R^3 is -H, and the other R^3 is either -H or -CH; and each m is 1.

5. The method of claim 3 wherein said compound has the chemical structure:



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wherein X^1 is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl;

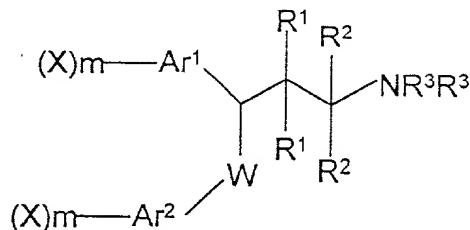
25 X^2 is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl; and

R^3 is either -H or -CH₃;

or a pharmaceutically acceptable salt thereof.

6. The method of claim 5, wherein X^1 is -F, -Cl, -OCF₃, or -CF₃; and X^2 is either 2-OCH₃, 2-CH₃, 3-F, 3-CF₃, or 4-CF₃.

7. A method of treating a patient for depression comprising the step of administering to said patient an effect amount of a compound having the chemical structure:



5

wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, and -O-acyl;

10 Ar¹ and Ar² are each independently selected from the group consisting of phenyl, naphthyl, thiofuranyl, tetrahydronaphthyl, furanyl, tetrahydrofuranyl, pyridyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl cyclohexyl, cycloheptyl, and cyclopentyl;

15 each R¹ is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R² is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R²'s together are imino;

each R³ is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl; and

20 m is 0 to 5;

or a pharmaceutically acceptable salt thereof.

8. The method of claim 7, wherein for said compound each X is independently either -F, -Cl, -OCF₃, or -CF₃;

25 Ar¹ and Ar² are each independently phenyl or naphthyl;

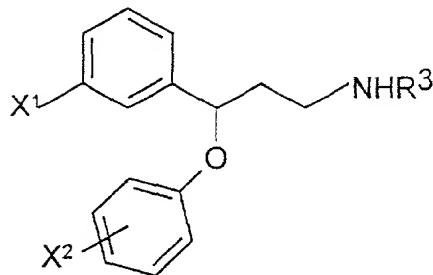
each R¹ is -H;

each R² is -H;

one R³ is -H, and the other R³ is either -H or -CH₃;

each m is 0 or 1.

9. The method of claim 7, wherein said compound has the chemical structure:



5 wherein X^1 is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl;

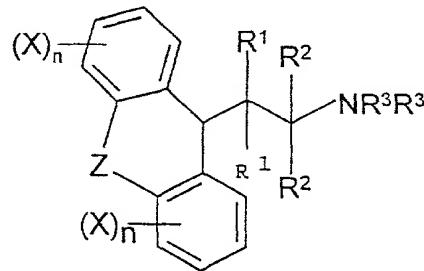
X^2 is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl; and

 R³ is either -H or -CH₃;

10 or a pharmaceutically acceptable salt thereof.

10. The method of claim 9 wherein X^1 is either -F, -Cl, -OCF₃ or -CF₃; and X^2 is either 2-OCH₃, 2-CH₃, 3-F, 3-CF₃, or 4-CF₃.

15 11. A method of treating a patient for depression comprising the step of administering to said patient an effective amount of a compound having the chemical structure:



20 wherein each X is independently selected from the group consisting of -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, and -O-acyl;

each R^1 is independently selected from the group consisting of -H, alkyl, hydroxyalkyl, -OH, -O-alkyl, and -O-acyl;

each R^2 is independently selected from the group consisting of -H, alkyl, and hydroxyalkyl, or both R^2 's together are imino;

5 each R^3 is independently selected from the group consisting of -H, alkyl, 2-hydroxyethyl, and alkylphenyl;

Z is either $-\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}(\text{CH}_3)-$, $-\text{CH}=\text{CH}-$, $-\text{O}-\text{CH}_2-$, $-\text{S}-\text{CH}_2-$, $-\text{CH}_2-$, $-\text{O}-$, or $-\text{S}-$; and

10 each n is independently 1 to 4; or a pharmaceutically acceptable salt thereof.

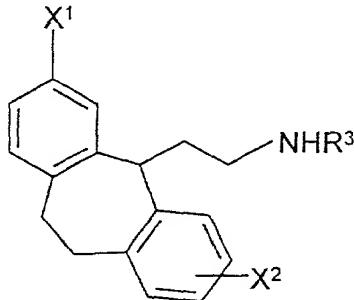
12. The compound of claim 11, wherein each X is independently either -F, -Cl, $-\text{OCF}_3$ or $-\text{CF}_3$;

each R^1 is -H;

each R^2 is -H;

15 one R^3 is -H, and the other R^3 is either -H or -CH; and each n is 1.

13. The method of claim 11, wherein said compound has the chemical structure:



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wherein X^1 is either -Br, -Cl, -F, -I, $-\text{CF}_3$, alkyl, -OH, $-\text{OCF}_3$, -O-alkyl, or -O-acyl;

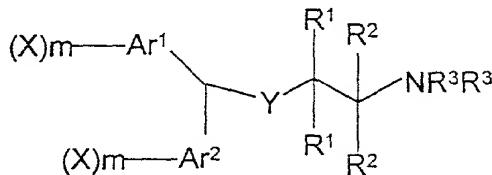
X^2 is either -Br, -Cl, -F, -I, $-\text{CF}_3$, alkyl, -OH, $-\text{OCF}_3$, -O-alkyl, or -O-acyl; and

25 R^3 is either -H or $-\text{CH}_3$;

or a pharmaceutically acceptable salt thereof.

14. The method of claim 13 wherein X^1 is $-F$, $-Cl$, $-OCF_3$, or $-CF_3$; and X^2 is either either $-F$, $-Cl$, $-OCH_3$, $-CH_3$, $-OCF_3$ or $-CF_3$.

5 15. A method of treating a patient for depression comprising the step of administering to said patient an effect amount of a compound having the chemical structure:



10 wherein each X is independently selected from the group consisting of $-Br$, $-Cl$, $-F$, $-I$, $-CF_3$, alkyl, $-OH$, $-OCF_3$, $-O$ -alkyl, and $-O$ -acyl; preferably, each X is independently either $-F$, $-Cl$, $-OCF_3$ or $-CF_3$;

15 Ar^1 and Ar^2 are each independently selected from the group consisting of phenyl, naphthyl, thiofuranyl, tetrahydronaphthyl, furanyl, tetrahydrofuranyl, pyridyl, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, cyclohexyl, cycloheptyl, and cyclopentyl; preferably Ar^1 and Ar^2 are independently naphthyl or phenyl; more preferably at least one of 20 Ar^1 and Ar^2 is phenyl; and more preferably, both Ar^1 and Ar^2 are phenyl;

25 Y is either $-CH_2-$, $-O-$, or $-S-$;

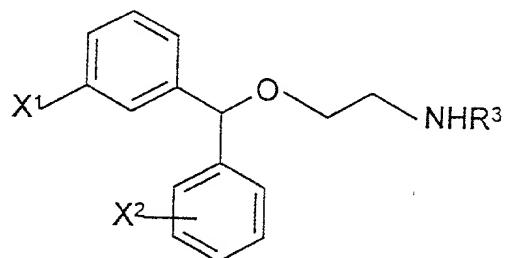
each R^1 is independently selected from the group consisting of $-H$, alkyl, hydroxyalkyl, $-OH$, $-O$ -alkyl, and $-O$ -acyl; 25 preferably, each R^1 is $-H$;

each R^2 is independently selected from the group consisting of $-H$, alkyl, and hydroxyalkyl, or both R^2 's together are imino; preferably each R^2 is $-H$;

30 each R^3 is independently selected from the group consisting of $-H$, alkyl, 2-hydroxyethyl, and alkylphenyl; preferably, each R^3 is independently either $-H$ or $-CH_3$; more preferably one R^3 is $-H$, and the other R^3 is either $-H$ or $-CH_3$; and

each m is independently an integer from 0 to 5; and preferably, each m is independently 0 or 1.

5 16. The method of claim 15, wherein said compound has the chemical structure; Structure VIII



wherein X^1 is independently selected from the group consisting of -H, -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, 10 -OCF₃, -O-alkyl, or -O-acyl; preferably, X^1 is either -F, -Cl, -OCF₃ and -CF₃;

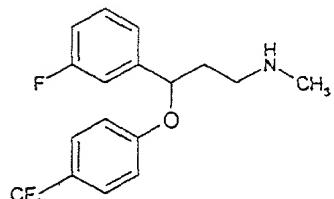
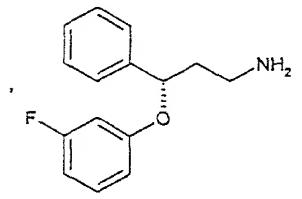
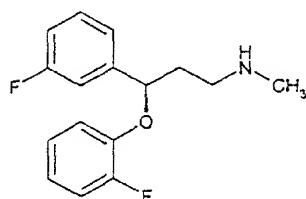
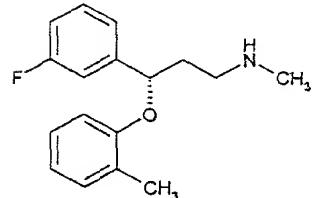
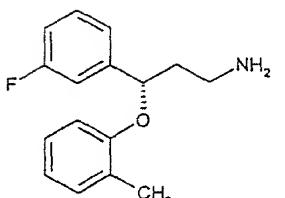
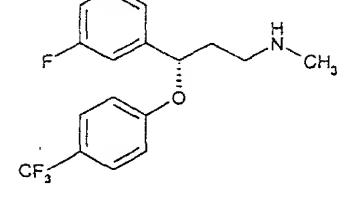
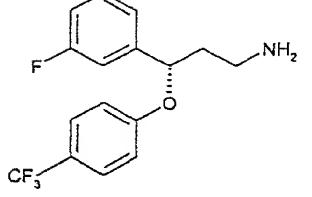
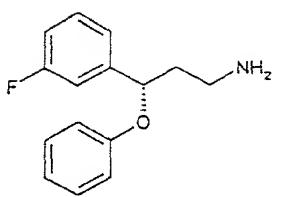
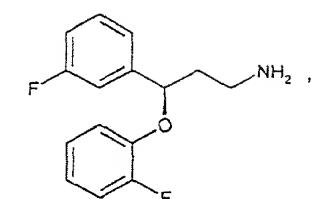
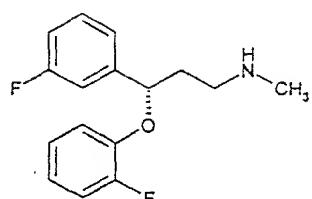
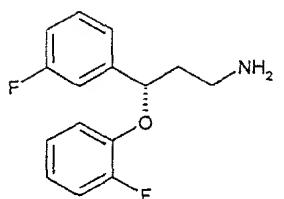
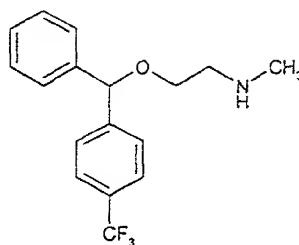
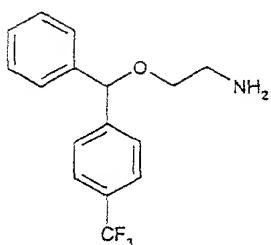
15 X^2 is either -Br, -Cl, -F, -I, -CF₃, alkyl, -OH, -OCF₃, -O-alkyl, or -O-acyl; preferably, X^2 is independently either -F, -Cl, -OCH₃, -CH₃, -OCF₃ or -CF₃; more preferably, X^2 is either 2-

15 OCH₃, 2-CH₃, 3-F, 3-CF₃, or 4-CF₃; and

R^3 is either -H or CH₃;

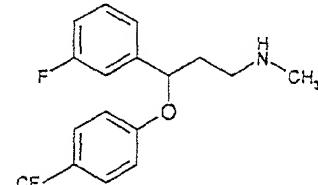
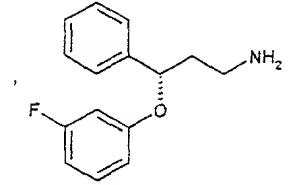
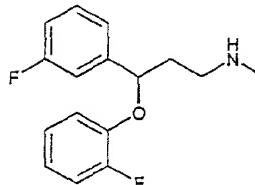
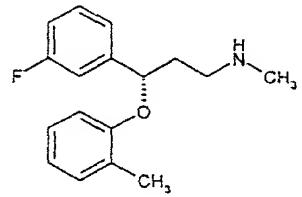
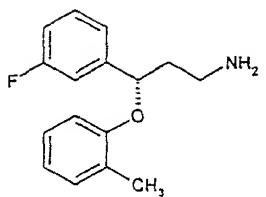
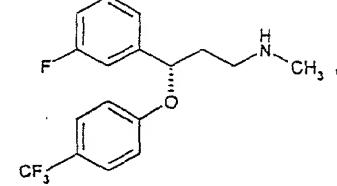
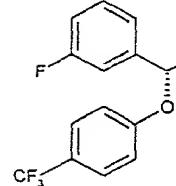
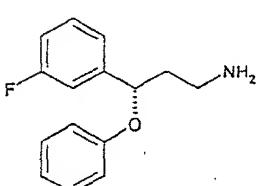
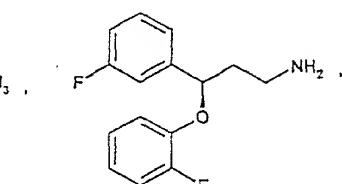
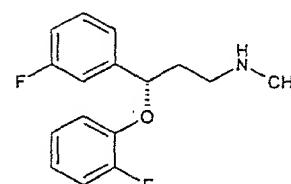
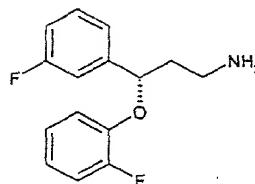
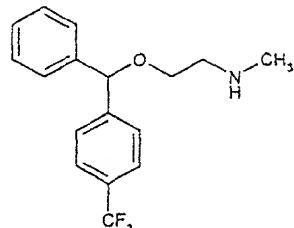
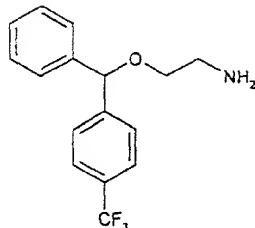
or a pharmaceutically acceptable salt thereof.

17. A compound having the chemical structure;



or a pharmaceutically acceptable salt thereof.

18. A method of treating a patient for depression comprising the step of administering to said patient an effect amount of a compound having the chemical structure:



5 or a pharmaceutically acceptable salt thereof.